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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent Examining Operations

Applicant(s):	Mosca	
Serial No:	09/638,358	Art Unit: 1632
Filed:	August 15, 2000	Examiner: Wehbe
Title:	Antigen Presenting Mesenchymal Stem Cells	
Docket No.:	640100-383	Customer No.: 27162

TRANSMITTAL LETTER

Commissioner for Patents
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Raymond J. Lillie 4/21/04
Raymond J. Lillie, Esq. **Date**

#217798 v1

Respectfully submitted,

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UNITED STATES PATENT AND TRADEMARK OFFICE

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BRIEF BEFORE THE BOARD OF APPEALS AND INTERFERENCES

SIR:

This is an appeal from the Final Rejection dated November 5, 2002.

Real Party in Interest

The real party in interest is Osiris Therapeutics, Inc., the assignee of the claimed subject matter of the above-identified application.

Related Appeals and Interferences

There are no related appeals or interferences.

Status of Claims

Claims 1-18 have been cancelled without prejudice.

Claims 19-39 are pending, stand finally rejected, and are before the Board on appeal. These claims are listed in the Appendix attached hereto.

Status of Amendments

An Amendment in response to the Final Rejection was filed on February 3, 2003. In such Amendment, Claims 1-18 were cancelled without prejudice, and Claims 19-39 were added. In an Advisory Action dated March 19, 2003, the Examiner indicated that the Amendment would be entered.

Summary of the invention

In one aspect of the present invention, there is provided, as defined broadly in Claim 19, a composition comprising a mesenchymal stem cell that expresses at least one co-stimulatory molecule, and has been modified to have at least one exogenous antigen fragment bound to a member selected from the group consisting of MHCII, MHCI, and CD1 such that the at least one antigen is presented to initiate an immune response.

In another aspect of the present invention, as defined in Claim 29, there is provided a composition comprising a cell of the adipocyte lineage that expresses at least one co-stimulatory molecule. The cell has been modified to have at least one exogenous antigen fragment bound to a primary surface molecule of the cell such that the antigen is presented to initiate an immune response.

The above aspects of the present invention are described in the specification at Page 6, lines 10-28.

As indicated in the first paragraph of Page 4 of the specification, professional antigen-presenting cells, or APCs, cannot be expanded into large populations and are difficult to engineer genetically.

In contrast, large members of mesenchymal stem cells can be produced from relatively small amounts of bone marrow. Also, mesenchymal stem cells and cells of the adipocyte lineage are more amenable to genetic engineering than professional APCs.

Issues Presented

The claims stand rejected under 35 U.S.C.103 as being unpatentable over Robinson, et al. in view of Gerson, et al.

It is the Examiner's position that, based on the motivation provided by Gerson to use transduced human mesenchymal stem cells for in vivo therapy, and the teachings of Robinson that any primary non-professional antigen presenting cells can be engineered to induce immune responses, it would have been prima facie obvious to the skilled artisan to use human mesenchymal stem cells as the primary non-professional antigen presenting cell in the methods of making engineered antigen presenting cells taught by Robinson.

The Examiner also has held that in view of the teachings in Gerson regarding the isolation, culturing, and genetic manipulation of mesenchymal stem cells, and the high level of skill in molecular biology at the time of filing, the skilled artisan would have a reasonable expectation of success in transfecting a mesenchymal stem cell with a vector encoding B7-1 or B7-2, and modifying the cell further to present an antigen bound to MHC Class II.

Grouping of Claims

The rejected claims do not stand or fall together.

The preset invention is directed to two aspects, defined broadly in Claims 19 and 29, respectively. For reasons including but not limited to those given hereinbelow, each of said two aspects is patentable over the cited prior art, and therefore the rejected claims do not and should not stand or fall together.

Argument

Robinson discloses the genetic modification of cells and cell lines *ex vivo* in order to render the cells capable of processing and presenting antigens to cells of the immune system of a subject, and to express different HLA molecules for matching to the HLA specificity of the subject. The cells also are modified to express immunoregulatory

molecules for directing the immune response of the subject. As indicated at Column 9, lines 31-45 of Robinson, cells which may be modified include macrophages, B-cells, monocytes, dendritic cells, Langerhans cells, activated T-cells, fibroblasts, eosinophils, keratinocytes, astrocytes, microglial cells, thymic cortical epithelial cells, endothelial cells, Schwann cells, retinal pigment epithelial cells, myoblasts, vascular smooth muscle cells, chondrocytes, enterocytes, thyrocytes, and kidney tubule cells.

Although Robinson discloses a multitude of types of cells that may be genetically engineered to render the cells capable of processing and presenting antigens to cells of the immune system of a subject, Robinson does not disclose or even remotely suggest to one of ordinary skill in the art a mesenchymal stem cell, as defined broadly in Claim 19, or a cell of the adipocyte lineage, as defined broadly in Claim 29,that expresses at least one co-stimulatory molecule, and has been modified to have at least one exogenous antigen fragment bound to a surface molecule. Robinson, therefore, does not render Applicant's invention as claimed obvious to one of ordinary skill in the art.

Gerson teaches that mesenchymal stem cells may be genetically engineered to express various therapeutic agents. Examples of therapeutic agents are given in Columns 8 and 9.

Gerson is directed to the use of mesenchymal stem cells which express therapeutic agents in order to treat diseases or disorders. Applicant, in contrast, provides mesenchymal stem cells, or cells of the adipocyte lineage, that express at least one co-stimulatory molecule, and have been modified to have at least one exogenous antigen fragment bound to a member selected from the group consisting of MHCII, MHCI, and CD1, such that the at least one antigen is presented to initiate an immune response.

Although Gerson discloses a multitude of therapeutic agents which may be expressed by mesenchymal stem cells, Gerson, however, does not disclose or even remotely suggest to one of ordinary skill in the art that one can make a composition which comprises a mesenchymal stem cell that expresses at least one co-stimulatory

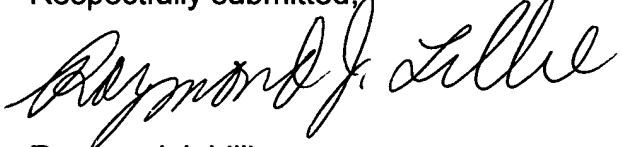
molecule, and has been modified to have at least one exogenous antigen fragment bound to a primary surface molecule. and which can present an antigen to initiate immune response. Thus, although Gerson discloses the genetic engineering of mesenchymal stem cells to express various therapeutic agents, Gerson does not render Applicant's claimed mesenchymal stem cells, as defined broadly in Claim 19, or cells of the adipocyte lineage, as defined broadly in Claim 29, obvious to one of ordinary skill in the art.

Applicant and only Applicant has provided a composition which comprises a mesenchymal stem cell as defined broadly in Claim 19, or a cell of the adipocyte lineage as defined broadly in Claim 29, that expresses at least one co-stimulatory molecule, and has been modified to have at least one exogenous antigen fragment bound to a primary surface of the cell, or bound to a member selected from the group consisting of MHCII, MHCI, and CD1, such that the at least one antigen is presented to initiate an immune response.

Robinson and Gerson, taken in combination, do not disclose or even remotely suggest to one of ordinary skill in the art Applicant's compositions as claimed. At best, the combination of Robinson and Gerson would render it obvious to try to provide Applicant's compositions as claimed; however, such a standard for obviousness is improper. (See Uniroyal, Inc. v. Rudkin-Wiley Corp., 5 U.S.P.Q.2d 1434 (C.A.F.C. 1988), at 1440; American Hospital Supply Corp. v. Travenol Laboratories, Inc., 223 U.S.P.Q. 577 (C.A.F.C. 1984), at 582; In Re Dow Chemical, 5 U.S.P.Q.2d 1529 (C.A.F.C. 1988), at 1531.) Therefore, Robinson and Gerson do not render Applicants' claimed compositions obvious to one of ordinary skill in the art.

For the above reasons and others, this application is in condition for allowance, and it is therefore respectfully requested that the rejection under 35 U.S.C.103 be reversed.

Respectfully submitted,



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APPENDIX-CLAIMS ON APPEAL

19. A composition comprising a mesenchymal stem cell that expresses at least one co-stimulatory molecule, and has been modified to have at least one exogenous antigen fragment bound to a member selected from the group consisting of MHCII, MHCI, and CD1 such that said at least one antigen is presented to initiate an immune response.

20. The composition of Claim 19 wherein said member is MHCII and said mesenchymal stem cell has been treated with interferon-γ.

21. The composition of Claim 20 wherein said mesenchymal stem cell further includes exogenous genetic material that encodes interferon-γ.

22. The composition of Claim 19 wherein the co-stimulatory molecule is selected from the group consisting of B7-1 and B7-2.

23. The composition of Claim 19 wherein the exogenous antigen is selected from the group consisting of a protein, a polypeptide, a glycolipid, and a lipid.

24. The composition of Claim 19 wherein the mesenchymal stem cell was modified by contact with the exogenous antigen fragment or an antigen including said fragment.

25. The composition of Claim 19 wherein the mesenchymal stem cell contains exogenous genetic material that encodes the exogenous antigen fragment or an antigen including said fragment.

26. The composition of Claim 25 wherein said exogenous genetic material is contained in an expression vector.

27. The composition of Claim 19 wherein the mesenchymal stem cell includes exogenous genetic material that encodes said at least one co-stimulatory molecule.

28. The composition of Claim 27 wherein said exogenous genetic material encoding said at least one co-stimulatory molecule is contained in an expression vector.

29. A composition comprising a cell of the adipocyte lineage that expresses at least one co-stimulatory molecule and has been modified to have at least one exogenous antigen fragment bound to a primary surface molecule of said cell such that said at least one antigen is presented to initiate an immune response.

30. The composition of Claim 29 wherein said primary surface molecule is selected from the group consisting of MHCII, MHCI, and CD1.

31. The composition of Claim 30 wherein said member is MHCII and said cell has been treated with interferon-γ.

32. The composition of Claim 31 wherein said cell further includes exogenous genetic material that encodes interferon-γ.

33. The composition of Claim 29 wherein the co-stimulatory molecule is selected from the group consisting of B7-1 and B7-2.

34. The composition of Claim 29 wherein the exogenous antigen is selected from the group consisting of a protein, a polypeptide, a glycolipid, and a lipid.

35. The composition of Claim 29 wherein the cell was modified by contact with the exogenous antigen fragment or an antigen including said fragment.

36. The composition of Claim 29 wherein the cell contains exogenous genetic material that encodes the exogenous antigen fragment or an antigen including said fragment.

37. The composition of Claim 36 wherein said exogenous genetic material is contained in an expression vector.

38. The composition of Claim 29 wherein the cell includes exogenous genetic material that encodes said at least one co-stimulatory molecule.

39. The composition of Claim 38 wherein said exogenous genetic material encoding said at least one co-stimulatory molecule is contained in an expression vector.